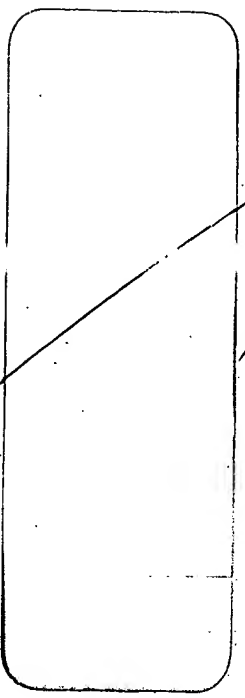
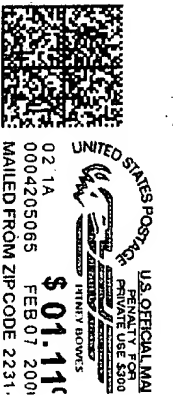
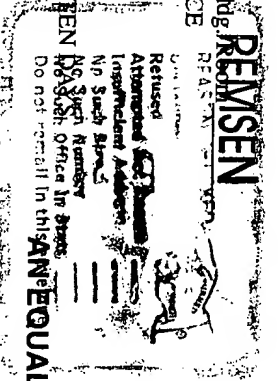
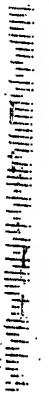


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## NOTICE OF ALLOWANCE AND FEE(S) DUE

6449 7590 02/07/2006  
ROTHWELL, FIGG, ERNST & MANBECK, P.C.  
1425 K STREET, N.W.  
SUITE 800  
WASHINGTON, DC 20005



EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	
DATE MAILED: 02/07/2006	

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,368	09/20/2001	Micko Katsuura	447.001	8538

TITLE OF INVENTION: BONE MORPHOGENETIC PROTEIN ANTAGONIST BASED ON THE MATURE PROTEIN

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$700	\$0	\$700	05/08/2006

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. **PROSECUTION ON THE MERITS IS CLOSED.** THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN **THREE MONTHS** FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. **THIS STATUTORY PERIOD CANNOT BE EXTENDED.** SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

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If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

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III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER:** Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.



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## NOTICE OF ALLOWANCE AND FEE(S) DUE

6449 7590 02/07/2006

ROTHWELL, FIGG, ERNST & MANBECK, P.C.  
1425 K STREET, N.W.  
SUITE 800  
WASHINGTON, DC 20005

EXAMINER

ROMEO, DAVID S

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 02/07/2006

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,368	09/20/2001	Micko Katsuura	447.001	8538

TITLE OF INVENTION: BONE MORPHOGENETIC PROTEIN ANTAGONIST BASED ON THE MATURE PROTEIN

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$700	\$0	\$700	05/08/2006

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**THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.**

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If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

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III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER:** Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

# PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: **Mail Stop ISSUE FEE**  
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**INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

6449 7590 02/07/2006  
**ROTHWELL, FIGG, ERNST & MANBECK, P.C.**  
**1425 K STREET, N.W.**  
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**Certificate of Mailing or Transmission**  
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,368	09/20/2001	Micko Katsuura	447.001	8538

TITLE OF INVENTION: BONE MORPHOGENETIC PROTEIN ANTAGONIST BASED ON THE MATURE PROTEIN

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$700	\$0	\$700	05/08/2006

EXAMINER	ART UNIT	CLASS-SUBCLASS
ROMEO, DAVID S	1647	530-350000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.563).  
☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.  
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list  
(1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_  
(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 \_\_\_\_\_  
3 \_\_\_\_\_

## 3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

## 4a. The following fee(s) are enclosed:

- ☐ Issue Fee  
☐ Publication Fee (No small entity discount permitted)  
☐ Advance Order - # of Copies \_\_\_\_\_

## 4b. Payment of Fee(s):

- ☐ A check in the amount of the fee(s) is enclosed.  
☐ Payment by credit card. Form PTO-2038 is attached.  
☐ The Director is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

## 5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

The Director of the USPTO is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above. NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_

Date \_\_\_\_\_

Typed or printed name \_\_\_\_\_

Registration No. \_\_\_\_\_

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/806,368	KATSUURA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	David S. Romeo	1647	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 10/25/2005.
2. ☒ The allowed claim(s) is/are 24-43.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☒ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☒ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

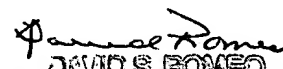
Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ol style="list-style-type: none"> <li>1. <input type="checkbox"/> Notice of References Cited (PTO-892)</li> <li>2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</li> <li>3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),<br/>Paper No./Mail Date _____</li> <li>4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br/>of Biological Material</li> </ol> | <ol style="list-style-type: none"> <li>5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</li> <li>6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),<br/>Paper No./Mail Date <u>200602</u>.</li> <li>7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment</li> <li>8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance</li> <li>9. <input type="checkbox"/> Other _____</li> </ol> |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

  
**DAVID S. ROMEO**  
**PRIMARY EXAMINER**

Art Unit: 1647

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Monica Kitts on January 26, 2006.

The application has been amended as follows:

**Listing of Claims:**

**Claims 1-23 (Canceled)**

24. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by replacing at least one methionine or tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO:1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification.
25. (New) The BMP antagonist according to claim 24, wherein the chemical modification for said tryptophan residue is an allylsulphenylation reaction.
26. (New) The BMP antagonist according to claim 25 in which two tryptophan residues are allylsulphenylated and having the amino acid sequence of SEQ ID NO 7.
27. (New) The BMP antagonist according to claim 24, wherein said mature human MP52 is a dimer protein.
28. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by converting at least one residue of tryptophan residues existing in the amino acid sequences of mature human BMP-2 (SEQ ID NO 2), mature human BMP-4 (SEQ ID NO 3) or mature human BMP-7 (SEQ ID NO 4) to a hydrophilic residue by chemical

Art Unit: 1647

modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue.

29. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by replacing at least one amino acid residue of three hydrophobic amino acid residues, among said hydrophobic amino acid residues relating to a receptor binding site in the amino acid sequences of mature human BMP-2 (SEQ ID NO 2), mature human BMP-4 (SEQ ID NO 3), or mature human BMP-7 (SEQ ID NO 4), which are located in positions corresponding to those of methionine residues located in 30<sup>th</sup>, 71<sup>st</sup>, and 74<sup>th</sup> positions of the amino acid sequence of mature human MP52 (SEQ ID NO 1) with a hydrophilic amino acid residue or a polar amino acid residue.

30. (New) The BMP antagonist according to claim 28, wherein said mature human BMP-2, mature human BMP-4, or mature human BMP-7 is a dimer protein.

31. (New) A therapeutic agent containing a BMP antagonist according to claim 24.

32. (New) A therapeutic agent for therapy of diseases due to the expression of MP52, BMP-2, BMP-4 and/or BMP-7 containing a BMP antagonist according to claim 24 as an effective ingredient.



33. (New) A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by converting at least one methionine residue existing in the receptor binding site of mature human MP52 (SEQ ID NO:1) by chemical modification, wherein said chemical modification for said methionine residue is an alkylation reaction.
34. (New) The BMP antagonist according to claim 33, wherein the alkylation reaction is S-carboxymethylation in which at least one methionine residue is S-carboxymethylated and having the amino acid sequence of SEQ ID NO 6.
35. (New) The BMP antagonist according to claim 33, wherein said mature human MP52 is a dimer protein.
36. (New) A therapeutic agent containing a BMP antagonist according to claim 33.
37. (New) A therapeutic agent for therapy of diseases due to the expression of MP52, BMP-2, BMP-4 and/or BMP-7 containing a BMP antagonist according to claim 33 as an effective ingredient.
38. (New) A method for antagonizing MP52, BMP-2, BMP-4 and BMP-7, comprising administering to a patient in need thereof, an effective amount of a mature modified protein according to claim 33.

39. (New) The method according to claim 38, wherein said patient is suffering from ectopic ossification which is due to ectopic expression of MP52, BMP-2, BMP-4 and/or BMP-7.

40. (New) The method according to claim 38, wherein said patient is suffering from a metabolic disease with calcification.

41. (New) The method according to claim 40, wherein said metabolic disease with calcification is calcification of arterial sclerosis.

42. (New) A mature modified protein obtained by replacing at least one methionine residue at position 30, 71 or 74 or at least one tryptophan residue existing in mature human MP52 (SEQ ID NO:1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification, wherein said mature modified protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

43. (New) A mature, modified protein obtained by replacing at least one methionine or at least one tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO 1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification, wherein said mature modified

Art Unit: 1647

protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

44. (New) A method for antagonizing MP52, BMP-2, BMP-4 and BMP-7, comprising administering to a patient in need thereof, an effective amount of a mature modified protein according to claim 24.

45. (New) The method according to claim 44, wherein said patient is suffering from ectopic ossification which is due to ectopic expression of MP52, BMP-2, BMP-4 and/or BMP-7.

46. (New) The method according to claim 44, wherein said patient is suffering from a metabolic disease with calcification.

47. (New) The method according to claim <sup>46</sup>~~47~~, wherein said metabolic disease with calcification is calcification of arterial sclerosis.

DR  
2/6/6

Art Unit: 1647

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO  
PRIMARY EXAMINER  
ART UNIT 1647

DSR  
FEBRUARY 6, 2006

<b>Interview Summary</b>	<b>Application No.</b> 09/806,368	<b>Applicant(s)</b> KATSUURA ET AL.	
	<b>Examiner</b> David S. Romeo	<b>Art Unit</b> 1647	

All participants (applicant, applicant's representative, PTO personnel):

(1) David S. Romeo. (3)\_\_\_\_\_.

(2) Monica Kitts. (4)\_\_\_\_\_.

Date of Interview: 06 February 2006.

Type: a) ☒ Telephonic b) ☐ Video Conference  
c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☒ Yes e) ☐ No.

If Yes, brief description: Proposed claim amendments.

Claim(s) discussed: \_\_\_\_\_.

Identification of prior art discussed: \_\_\_\_\_.

Agreement with respect to the claims f) ☒ was reached. g) ☐ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: See Continuation Sheet.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

\_\_\_\_\_  
Examiner's signature, if required

## Summary of Record of Interview Requirements

### Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

### Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

#### Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

#### 37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,  
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

### Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: The reply filed 10/25/2005 is a complete reply to all the outstanding issues. The examiner proposed the following amendment in order to overcome new issues concerning the spontaneous oxidation of Met residues to the sulfoxide and then to the sulfone. In response, Ms. Kitts proposed the current examiner's amendment, which the examiner indicated was acceptable.  
Proposed examiner's amendment:

Cancel claims 2 and 3.

Replace claim 4 with the following claim:

4. A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by converting at least one methionine residue existing in the receptor binding site of mature human MP52 (SEQ ID NO: 1) by chemical modification, wherein the chemical modification for said methionine residue is an alkylation reaction.

Replace claim 16 with the following claim:

16. A BMP antagonist with antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 obtained by replacing at least one methionine or tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO: 1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification.

Replace claim 18 with the following claim:

18. A mature modified protein obtained by replacing at least one methionine residue at position 30, 71 or 74 or at least tryptophan residue existing in mature human MP52 (SEQ ID NO: 1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification, wherein said mature modified protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

Replace claim 19 with the following claim:

19. A mature, modified protein obtained by replacing at least one methionine residue or at least tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO: 1) with a hydrophilic amino acid residue or a polar amino acid residue, or converting said tryptophan residues to a hydrophilic residue by chemical modification, wherein said mature modified protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7..